

## REMARKS

Claims 5, 9, 12-14, 39, 42 and 50-59 are pending upon entry of the above amendments. Claim 10 has been cancelled. Claims 9, 39 and 42 have been amended to correct typographical errors and to more distinctly point out what the Applicants believe is their invention. No new matter has been introduced.

### Rejection under 35 U.S.C. §101

Claims 5, 9-10, 12-14, 39, 42 and 50-59 are rejected under 35 U.S.C. §101. The Examiner alleges that “the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention.” The Examiner further states that claims 12-14 are drawn to vector/expression vector comprising the nucleic acid of claim 5, wherein the vector is introduced into host cells to express the protein (claim 14) and claims 54-56 are drawn to vector/expression vector comprising nucleic acid of claim 9 while the specification fails to provide specific recombinant host cells comprising the vectors demonstrating expression of the nucleic acid. The Examiner also states that claims 39 and 42 are drawn to a pharmaceutical composition and kit, however that the specification does not indicate the function of the nucleic acids and one of skill in the art wouldn’t know how to use invention.

Applicant respectfully traverses this rejection. Under 35 U.S.C. §101, what is required is the assertion of a utility that is specific, substantial and credible. Applicants have asserted such a utility for the claimed invention in the specification. For example, in Example 2 beginning at page 194 of the specification, the expression of genes of the invention were assessed quantitatively in RNA samples from a variety of normal and pathological cells, cell lines and tissues by real time quantitative PCR (RTQ PCR). Results for NOV 4, nucleic acid encoding SEQ ID NO:14, are found in Example 2, section D, pages 220-230. More specifically, the Examiner is invited to review Panel 2D results are presented in Table 12DE at pages 223-225 and summarized on page 229. A description of the sources of the RNA samples used in Panel 2D may be found on page 197-198. On page 229 the specification teaches:

“highest expression of the CG50301-01 gene in ovarian cancer. The level of expression of this gene appears to be increased in some lung and gastric cancer tissue samples when compared to the matched normal tissue. The reverse appears to be true for kidney, where

expression is slightly higher in 6 of 9 normal tissues than in the matched cancer tissues. Thus, based upon its profile, the expression of this gene could be of use as a marker for distinguishing these cancers from the normal adjacent tissue or as a marker for different grades/ types of cancer.”

One of skill in the art, having read the specification, would therefore know to detect and compare the amount of expression of the nucleotide encoding SEQ ID NO:14 in samples of malignant and normal tissues, by using, e.g. RTQ-PCR methods as described in the specification to differentiate malignant tissues from normal tissues.

The utility described above is specific and substantial. Applicants have not suggested that NOV4 be used in a general undefined way or for diagnosing an unspecified disease. The specification teaches that the nucleic acid encoding the polypeptide of SEQ ID NO:14 may be used as a specific target for detecting expression, particularly in ovarian, lung, gastric, and kidney, tissue, to differentiate normal tissue from malignant tissue. Furthermore, the specification teaches that not any nucleic acid but specifically NOV4 may be used for this purpose. Since Applicants have made an assertion that the claimed invention is useful for a particular purpose, and such assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility is not proper. Applicants respectfully request the rejection be withdrawn.

#### **Rejections under 35 U.S.C. § 112, first paragraph**

Claims 5, 9-10, 12-14, 39, 42 and 50-59 are rejected under 35 U.S.C. §112 first paragraph as allegedly not supported by either a specific and substantial asserted utility or a well established utility.

Applicants respectfully disagree. As discussed above, a specific and substantial utility for the claimed invention is taught in the specification. Applicants respectfully request that the rejection be withdrawn.

Claims 5, 9-10, 51-53 and 57-59 in so much as they are directed to polynucleotide variants of SEQ ID NO:13 encoding polypeptide of SEQ ID NO:14 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention. The

pending claims refer to variants wherein one amino acid residue differs from the sequence of SEQ ID NO:14.

Applicants respectfully disagree. As explained in the specification and as appreciated by those skilled in the art, DNA sequence polymorphisms that lead to changes in the amino acid sequence of a gene exist within a population. Also as understood in the art, single amino acids can be altered from the wild-type sequence. Conservative amino acid substitutions can be made in the sequence. Example 3 in the specification at page 291 describes methods for identifying one type of such variant, single nucleotide polymorphisms (SNP) and NOV4 SNP sequences are described on page 294 demonstrating that Applicants were in possession of the claimed invention at the time of filing. Applicants respectfully submit that the rejection should be withdrawn.

### **Rejections under 35 U.S.C. §112, second paragraph**

Claim 10 is rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. While Applicants do not concede to the Examiner's position, to expedite prosecution of this application claim 10 has been canceled herein.

### **Rejection under 35 U.S.C. § 102**

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 U.S.C. §102(b) by the Examiner as anticipated by Schaefer et al. The Examiner contends that Schaefer et al. teaches a member of the Heregulin superfamily having a 99.77% sequence identity to amino acid sequence SEQ ID NO:14, residues 1-400; a 100% sequence identity to SEQ ID NO:14 residues 450-520; a variant having 99.5% sequence identity to SEQ ID NO:14, residues 1-400 wherein position 28 is Asp, position 64 is Val, position 76 is Ala.

Applicant strongly disagrees. Schaefer's gamma Heregulin protein is 768 amino acids long compared to SEQ ID NO:14 which is 2769 amino acids in length. While amino acid residues 1-560 match that of SEQ ID NO:14 with 99.8% sequence identity, over its entire length, Schaefer's protein has only a 20.2% sequence identity with SEQ ID NO:14. Schaefer teaches protein that at best has a domain in common with Applicant's protein and clearly does not anticipate Applicant's nucleic acid molecule of claim 5, 10, 12-14, 39, 42 or 50-53.

Furthermore, Applicants' fragments 1-400, 450-520, 750-850, 1100-1200, 1250-1400, 1490-1750, 1760-2300, 2400-2600, and 2650-2725 are not specifically taught by Schaefer and therefore can not be anticipated.

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 U.S.C. §102(b) by the Examiner as anticipated by Oohashi et al. The Examiner contends that Oohashi et al. teaches a protein having 98% sequence identity to SEQ ID NO:14, residues 750-850; having 98.1% sequence identity to SEQ ID NO:14 residues 1250-1400; having 99% sequence identity to SEQ ID NO:14 residues 1490-1750.

Applicants respectfully disagree. Oohashi's mouse protein has 97.1% sequence identity with Applicant's protein sequence. As the Examiner has stated, Oohashi's sequence is 98%, 98.1% and 99% identical to SEQ ID NO:14 residues 750-850; 1250-1400 and 1490-1750 respectively. Oohashi's sequence is not 100% identical to Applicant's claimed sequences and therefore does not anticipate pending claims 5, 10, 12-14, 39, 42 or 50-53.

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 U.S.C. §102(b) by the Examiner as anticipated by Wang et al. The Examiner contends that Wang et al teaches a nuclear protein having 99.1% sequence identity to SEQ ID NO:14 residues 1100-1200.

Applicants respectfully disagree. Wang et al's mouse sequence has 94% sequence identity over its full length and as the Examiner has offered, at best is only 99.1% identical to a fragment 1100-1200 of Applicant's SEQ ID NO:14. Wang's sequence is not identical to Applicant's claimed sequences and therefore does not anticipate Applicant's pending claims 5, 10, 12-14, 39, 42 or 50-53.

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 U.S.C. §102(b) by the Examiner as anticipated by Nagase et al. The Examiner contends that Nagase et al. teaches a protein having 100% sequence identity to SEQ ID NO:14 residues 1760-2300 and residues 2650-2725.

Applicant respectfully disagrees. Nagase's protein matches applicants only in the region of SEQ ID NO:14 residues 1697 to 2769. Overall Nagase's protein has only 38.8% sequence identity with Applicant's protein. Nagase clearly teaches a different protein with at best a domain

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in common with Applicant's. Nagase clearly does not anticipate Applicant's claimed sequences in pending claims 5, 10, 12-14, 39, 42 or 50-53. Applicant respectfully requests this rejection be withdrawn. Furthermore, Applicants' fragments 1-400, 450-520, 750-850, 1100-1200, 1250-1400, 1490-1750, 1760-2300, 2400-2600, and 2650-2725 are not specifically taught by Nagase and therefore can not be anticipated.

For any reference to anticipate the claimed invention under 35 U.S.C. 102, the claimed invention must be substantially identically disclosed in such reference. None of the references relied upon by the Examiner disclose a sequence identical to Applicant's claimed invention. Therefore the rejection must be withdrawn.

## CONCLUSION

Applicant respectfully requests that the amendments and remarks made herein be entered and made of record in the file history of the present application. Applicant respectfully submits that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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Dated: February 15, 2005